Dkt. 30435.54USD3 SBA/RDG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	Robert E. Reiter, et al.	
Serial No.:	not yet known	Examiner: Larry R. Helms
Filed:	herewith	Group Art Unit: 1642
Title:	PSCA: PROSTATE STEM CELL ANTIGEN AND USES THEREOF	

35 North Arroyo Parkway
Pasadena, California 91103
August 21, 2001

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

PRELIMINARY AMENDMENT

Please amend the subject application as follows.

IN THE CLAIMS:

Please cancel claims 2-52 without prejudice to pursue the subject matter of these claims in a continuation application to be filed in the future.

Please add new claims 53-88 as follows.

-- 53. (new) An antibody which competes for binding to the same epitope as the epitope bound by the monoclonal antibody designated 1G8, 2A2, 2H9, 3C5, 3E6, 3G3 or 4A10,

produced by the hybridomas designated HB-12612, HB-12613, HB-12614, HB-12616, HB-12618, HB-12615, or HB-12617, respectively, as deposited with the American Type Culture Collection.--

-- 54. (new) The antibody of claim 53 which is a monoclonal antibody.--

-- 55. (new) The antibody of claim 53 which is a polyclonal antibody.--

-- 56. (new) The antibody of claim 53 which is a chimeric antibody.--

-- 57. (new) The antibody of claim 56, wherein the chimeric antibody is a humanized antibody.--

-- 58. (new) A cell that produces the monoclonal antibody of claim 53.--

-- 59. (new) A recombinant protein comprising the antigen binding region of the antibody of claim 53.--

-- 60. (new) An Fab, F(ab')2 or Fv fragment of the antibody of claim 53.--

-- 61. (new) An immunoconjugate comprising a cytotoxic agent and the antibody of claim 53.--

-- 62. (new) An immunoconjugate comprising a cytotoxic agent and the recombinant protein of claim 59.--

-- 63. (new) The immunoconjugate of claim 61 or 62, wherein the cytotoxic agent is selected from a group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, abrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin,

retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, maytansinoids, and glucocorticoidricin.--

-- 64. (new) A method for detecting the presence of a PSCA protein in a sample comprising contacting the sample with the antibody of claim 53 and detecting the binding of the antibody with the PSCA protein in the sample.--

-- 65. (new) The method of claim 64, wherein the detecting comprises:

a. contacting the sample with the antibody capable of forming a complex with the PSCA protein in the sample; and

b. determining whether any complex is so formed.

-- 66. (new) A method for detecting the presence of a PSCA protein in a sample comprising contacting the sample with the recombinant protein of claim 57 and detecting the binding of the recombinant protein with the PSCA protein in the sample.--

-- 67. (new) The method of claim 66, wherein the detecting comprises:

a. contacting the sample with the recombinant protein capable of forming a complex with the PSCA protein in the sample; and

b. determining whether any complex is so formed.--

-- 68. (new) The method of claim 64 or 66, wherein the sample is a tissue or biological fluid.--

-- 69. (new) The method of claim 68, wherein the tissue is bone, bone marrow, bladder tissue, prostate tissue, colon cells, or pancreatic neuroendocrine cells.--

-- 70. (new) The method of claim 68, wherein the biological fluid is urine or blood serum. --

-- 71. (new) The method of claim 64, wherein the antibody is labeled so as to produce a detectable signal with a compound selected from the group consisting of a radiolabel, an enzyme, a chromophore and a fluorescer.--

-- 72. (new) The method of claim 66, wherein the recombinant protein is labeled so as to produce a detectable signal with a compound selected from the group consisting of a radiolabel, an enzyme, a chromophore and a fluorescer.--

-- 73. (new) A method for monitoring the course of any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer in a subject which comprises quantitatively determining in a first sample from the subject the presence of a PSCA protein by the method of claim 64 or 66 and comparing the amount so determined with the amount present in a second sample from the subject, such samples being taken at different points in time, a difference in the amounts determined being indicative of the course of the cancer.

-- 74. (new) A method for diagnosing in a subject any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer which comprises quantitatively determining in a cell sample from the subject the number of cells associated with the PSCA protein using the antibody of claim 53 and comparing the number of cells so determined to the amount in a sample from a normal subject, the presence of a measurable different amount indicating the presence of the cancer.--

-- 75. (new) A method for diagnosing in a subject any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer which comprises quantitatively determining in a cell sample from the subject the number of cells associated with the PSCA protein using the recombinant protein of claim 59 and comparing the number of cells so determined to the amount in a sample from a normal subject, the presence of a measurable different amount indicating the presence of the cancer.--

-- 76. (new) A method for diagnosing in a subject any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer which comprises quantitatively determining in a sample from the subject the amount of PSCA protein expressed by the cells using the antibody of claim 53 and comparing the amount so determined to the amount in a sample from a normal subject, the presence of a measurable different amount indicating the presence of the cancer.--

-- 77. (new) A method for diagnosing in a subject any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer which comprises quantitatively determining in a sample from the subject the amount of PSCA protein expressed by the cells using the recombinant protein of claim 59 and comparing the amount so determined to the amount in a sample from a normal subject, the presence of a measurable different amount indicating the presence of the cancer.--

-- 78. (new) The method of claim 76 or 77, wherein the sample is a cell sample or a biological fluid sample. --

-- 79. (new) The method of claim 78, wherein the cell sample is a tissue sample from bone, bone marrow, or prostate tissue. --

-- 80. (new) The method of claim 78, wherein the biological fluid is urine or blood serum. --

-- 81. (new) A method for selectively inhibiting a cell expressing PSCA antigen comprising reacting the immunoconjugate of claim 61 or 62 with the cell in an amount sufficient to inhibit the cell.--

-- 82. (new) A method of inhibiting the growth of tumor cells expressing PSCA comprising administering to a subject the antibody of claim 53 which binds specifically to the

extracellular domain of PSCA in an amount effective to inhibit growth of the tumor cells.--

-- 83. (new) The method of claim 82, wherein said antibody is conjugated to a cytotoxic agent.--

-- 84. (new) The method of claim 83, wherein said cytotoxic agent is a radioactive isotope. --

-- 85. (new) The method of claim 83, wherein said cytotoxic agent is selected from the group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid.--

-- 86. (new) The method of claim 84, wherein said radioactive isotope is selected from the group consisting of ^{212}Bi, ^{131}I, ^{131}In, ^{90}Y and ^{186}Re.--

-- 87. (new) A pharmaceutical composition useful in killing human cells expressing the PSCA antigen on the cell surface, comprising a pharmaceutically effective amount of the antibody of claim 53 and a pharmaceutically acceptable carrier. --

-- 88. (new) A kit comprising the antibody of claim 53 and a detectable label.--

REMARKS

Claims 1-52 were pending. Applicants canceled claims 2-52 and added new claims 53-88. Accordingly, claim 1 and new claims 53-88 are being examined.

Support for new claims 53-88 may be found in the application as originally filed. Accordingly, these changes do not involve new matter and applicants respectfully request entry of these changes.

Support for new claim 53 may be found in the specification at page 27, lines 29-31, page 28, lines 1-3, page 33, lines 8-13 and in originally filed claims 12 and 13.

Support for new claim 54 may be found in the specification at page 6, lines 6-7, page 24, lines 7-8 and in originally filed claim 9.

Support for new claim 55 may be found in the specification at page 6, lines 6-7 and page 24, lines 7-8 and page 32, lines 2-5.

Support for new claim 56 may be found in the specification at page 24, lines 7-8, page 28, lines 5-30 and in originally filed claim 11.

Support for new claim 57 may be found in the specification at page 24, lines 7-8, page 32, lines 5-15 and in originally filed claims 35-37.

Support for new claim 58 may be found in the specification at page 27, lines 29-31, page 28, lines 1-3, page 115, lines 15-29.

Support for new claim 59 may be found in the specification at page 24, lines11-15, page 35, lines 8-25.

Support for new claim 60 may be found in the specification at page 25, line 26, page 32, line 3 and in originally filed claim 15.

Support for new claim 61 may be found in originally filed claims 17-23.

Support for new claim 62 may be found in originally filed claims 18, 19 and 23.

Support for new claim 63 may be found in the specification at page 34, lines 26-31, page 35, lines 1-6 and in originally filed claim 24.

Support for new claim 64 may be found in the specification at page 25, lines 26-31; page 26, lines 1-8; page 48, lines 14-23; page 49, lines 1-11, 25-30; and page 50, lines 1-3.

Support for new claim 65 may be found in the specification at page 48, lines 14-23 and page 50, lines 5-10, 23-31.

Support for new claim 66 may be found in the specification at page 25, lines 26-31, page 26, lines 1-8, page 48, lines 14-23, page 49, lines 1-11, 25-30 and page 50, lines 1-3.

Support for new claim 67 may be found in the specification at page 48, lines 14-23 and page 50, lines 5-10, 23-31.

Support for new claim 68 may be found in the specification at page 48, lines 14-23 page 50, lines 23-31 and page 51, lines 6-9.

Support for new claim 69 may be found in the specification at page 25, lines 26-31, page 49, lines 1-11 and page 51, lines 19-31.

Support for new claim 70 may be found in the specification at page 48, lines 13-23 and page 51, lines 6-9.

Support for new claim 71 may be found in the specification at page 34, lines 13-19, page 37, lines 9-14 and page 51, lines 11-15.

Support for new claim 72 may be found in the specification at page 34, lines 13-19, page 37, lines 9-14 and page 51, lines 11-15.

Support for new claim 73 may be found in the specification at page 25, lines 24-31, page 49, lines 1-11.

Support for new claim 74 may be found in the specification at page 25, lines 12-31 and page 63, lines 11-19.

Support for new claim 75 may be found in the specification at page 25, lines 12-31 and page 63, lines 11-19.

Support for new claim 76 may be found in the specification at page 25, lines 12-24, page 30, 4-10, page 49, lines 25-30.

Support for new claim 77 may be found in the specification at page 25, lines 12-24, page 30, 4-10, page 49, lines 25-30.

Support for new claim 78 may be found in the specification at page 48, lines 17-18, page 49, lines 29-30 and page 51, lines 3-7.

Support for new claim 79 may be found in the specification at page 25, lines 26-31 and page 49, lines 25-29.

Support for new claim 80 may be found in the specification at page 49, lines 29-30 and page 51, lines 6-7.

Support for new claim 81 may be found in the specification at page, 62, lines 8-17, 30-31, page 63, lines 1-3 and in originally filed claim 48.

Support for new claim 82 may be found in the specification at page 51, lines 27-31, page 52, lines 1-8, page 53, lines 19-27 and in originally filed claims 29 and 48.

Support for new claim 83 may be found in the specification at page 34, lines 13-31, page 35, lines 1-6 and page 48, lines 6-12 and in originally filed claim 30.

Support for new claim 84 may be found in the specification at page 29, lines 18-19, page 34, lines 26-31 and page 35, lines 1-2 and in originally filed claim 32.

Support for new claim 85 may be found in the specification at page 34, lines 26-31, page 35, lines 1-6 and in originally filed claim 31.

Support for new claim 86 may be found in the specification at page 35, lines 1-2 and in originally filed claim 33.

Support for new claim 87 may be found in the specification at page 58, lines 20-27, page 79, lines 1-21 and in originally filed claims 25-26.

Support for new claim 88 may be found in the specification at page 51, lines 11-15.

No fee is deemed necessary in connection with the filing of this Preliminary Amendment. If any fee is necessary, the Patent Office is authorized to charge any additional fee to Deposit Account No. 50-0306.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please cancel claims 2-52 without prejudice to pursue the subject matter of these claims in a continuation application to be filed in the future.

Please add new claims 53-88 as follows.

-- 53. (new) An antibody which competes for binding to the same epitope as the epitope bound by the monoclonal antibody designated 1G8, 2A2, 2H9, 3C5, 3E6, 3G3 or 4A10, produced by the hybridomas designated HB-12612, HB-12613, HB-12614, HB-12616, HB-12618, HB-12615, or HB-12617, respectively, as deposited with the American Type Culture Collection.--

-- 54. (new) The antibody of claim 53 which is a monoclonal antibody.--

-- 55. (new) The antibody of claim 53 which is a polyclonal antibody.--

-- 56. (new) The antibody of claim 53 which is a chimeric antibody.--

-- 57. (new) The antibody of claim 56, wherein the chimeric antibody is a humanized antibody.--

-- 58. (new) A cell that produces the monoclonal antibody of claim 53.--

-- 59. (new) A recombinant protein comprising the antigen binding region of the antibody of claim 53.--

-- 60. (new) An Fab, F(ab')2 or Fv fragment of the antibody of claim 53.--

-- 61. (new) An immunoconjugate comprising a cytotoxic agent and the antibody of claim 53.--

-- 62. (new) An immunoconjugate comprising a cytotoxic agent and the recombinant protein of claim 59.--

-- 63. (new) The immunoconjugate of claim 61 or 62, wherein the cytotoxic agent is selected from a group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, abrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, maytansinoids, and glucocorticoidricin.--

-- 64. (new) A method for detecting the presence of a PSCA protein in a sample comprising contacting the sample with the antibody of claim 53 and detecting the binding of the antibody with the PSCA protein in the sample.--

-- 65. (new) The method of claim 64, wherein the detecting comprises:

a. contacting the sample with the antibody capable of forming a complex with the PSCA protein in the sample; and

b. determining whether any complex is so formed.

-- 66. (new) A method for detecting the presence of a PSCA protein in a sample comprising contacting the sample with the recombinant protein of claim 57 and detecting the binding of the recombinant protein with the PSCA protein in the sample.--

-- 67. (new) The method of claim 66, wherein the detecting comprises:

a. contacting the sample with the recombinant protein capable of forming a complex with the PSCA protein in the sample; and

b. determining whether any complex is so formed.--

-- 68. (new) The method of claim 64 or 66, wherein the sample is a tissue or biological fluid.--

-- 69. (new) The method of claim 68, wherein the tissue is bone, bone marrow, bladder tissue, prostate tissue, colon cells, or pancreatic neuroendocrine cells.--

-- 70. (new) The method of claim 68, wherein the biological fluid is urine or blood serum. --

-- 71. (new) The method of claim 64, wherein the antibody is labeled so as to produce a detectable signal with a compound selected from the group consisting of a radiolabel, an enzyme, a chromophore and a fluorescer.--

-- 72. (new) The method of claim 66, wherein the recombinant protein is labeled so as to produce a detectable signal with a compound selected from the group consisting of a radiolabel, an enzyme, a chromophore and a fluorescer.--

-- 73. (new) A method for monitoring the course of any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer in a subject which comprises quantitatively determining in a first sample from the subject the presence of a PSCA protein by the method of claim 64 or 66 and comparing the amount so determined with the amount present in a second sample from the subject, such samples being taken at different points in time, a difference in the amounts determined being indicative of the course of the cancer.

-- 74. (new) A method for diagnosing in a subject any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer which comprises quantitatively determining in a cell sample from the subject the number of cells associated with the PSCA protein using the antibody of claim 53 and comparing

the number of cells so determined to the amount in a sample from a normal subject, the presence of a measurable different amount indicating the presence of the cancer.--

-- 75. (new) A method for diagnosing in a subject any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer which comprises quantitatively determining in a cell sample from the subject the number of cells associated with the PSCA protein using the recombinant protein of claim 59 and comparing the number of cells so determined to the amount in a sample from a normal subject, the presence of a measurable different amount indicating the presence of the cancer.--

-- 76. (new) A method for diagnosing in a subject any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer which comprises quantitatively determining in a sample from the subject the amount of PSCA protein expressed by the cells using the antibody of claim 53 and comparing the amount so determined to the amount in a sample from a normal subject, the presence of a measurable different amount indicating the presence of the cancer.--

-- 77. (new) A method for diagnosing in a subject any of the cancers selected from the group consisting of prostate cancer, bladder carcinoma and bone metastases of prostate cancer which comprises quantitatively determining in a sample from the subject the amount of PSCA protein expressed by the cells using the recombinant protein of claim 59 and comparing the amount so determined to the amount in a sample from a normal subject, the presence of a measurable different amount indicating the presence of the cancer.--

-- 78. (new) The method of claim 76 or 77, wherein the sample is a cell sample or a biological fluid sample. --

-- 79. (new) The method of claim 78, wherein the cell sample is a tissue sample from bone, bone marrow, or prostate tissue. --

-- 80. (new) The method of claim 78, wherein the biological fluid is urine or blood serum. --

-- 81. (new) A method for selectively inhibiting a cell expressing PSCA antigen comprising reacting the immunoconjugate of claim 61 or 62 with the cell in an amount sufficient to inhibit the cell.--

-- 82. (new) A method of inhibiting the growth of tumor cells expressing PSCA comprising administering to a subject the antibody of claim 53 which binds specifically to the extracellular domain of PSCA in an amount effective to inhibit growth of the tumor cells.--

-- 83. (new) The method of claim 82, wherein said antibody is conjugated to a cytotoxic agent.--

-- 84. (new) The method of claim 83, wherein said cytotoxic agent is a radioactive isotope. --

-- 85. (new) The method of claim 83, wherein said cytotoxic agent is selected from the group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid.--

-- 86. (new) The method of claim 84, wherein said radioactive isotope is selected from the group consisting of ^{212}Bi, ^{131}I, ^{131}In, ^{90}Y and ^{186}Re.--

-- 87. (new) A pharmaceutical composition useful in killing human cells expressing the PSCA antigen on the cell surface, comprising a pharmaceutically effective amount of the antibody of claim 53 and a pharmaceutically acceptable carrier. --

-- 88. (new) A kit comprising the antibody of claim 53 and a detectable label.--